REMARKS

Reconsideration of this application in view of the above amendments and following remarks is respectfully requested. Prior to the present amendment, claims 1, 15-17, and 40-43 were pending, with claims 40-43 withdrawn from consideration. By the present amendment, claims 40-43 are cancelled. Claim 1 is amended to more specifically recite particular embodiments of the present invention. Claim 17 is also amended to more specifically describe one aspect of the claimed invention, and new claims 44 and 45 are added to describe particular embodiments of this aspect of the invention. Support for these amendments may be found throughout the specification and claims as originally filed. Support for biotinylated proteins comprising a biotinylation sequence motif is provided throughout the instant specification, including, *e.g.*, at page 51, lines 12-16, and page 23, line 22, to page 24, line 3. Support for chips adapted for use in the recited detection devices is provided, *e.g.*, at page 55, line 25, to page 56, line 19. Therefore, the amendments do not constitute new matter.

It should be noted that the above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation, or continuation-in-part application. Upon entry of the present amendment, claims 1, 15-17, 44, and 45 will be pending.

Telephone Interview

Applicants appreciate the Examiner conducting a telephone interview on June 20, 2006 with their representative to clarify the remaining bases of rejection and discuss potential amendments to overcome these rejections. The present amendment has been prepared in light of this telephone interview, and the claim amendments made herein conform to those that the Examiner indicated would likely overcome the outstanding rejections. Specifically, claim 1 has been amended to incorporate the feature previously recited in claim 40, and claim 17 has been amended to explicitly recite structural features, as suggested by the Examiner.

Election/Restrictions

Claims 40-43 have been withdrawn from consideration by the Examiner as being directed to a non-elected invention. In order to expedite prosecution of the instant application, claims 40-43 are canceled by the present amendment, and the feature of claim 40, namely that the polypeptide comprises a biotinylation sequence motif, has been incorporated into claim 1.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 17, which depends from claim 1, stands rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. More specifically, the Examiner alleges that this claim is drawn to a receptor chip that is adapted for detection using a particular method, but it is unclear how the adaption affects the structure of the product of claim 1.

Applicants traverse this basis of rejection and submit that the skilled artisan would readily appreciate that receptor chips adapted for the various recited detection methods possess additional characteristics as compared to the receptor chip of claim 1. Nonetheless, in order to expedite prosecution, claim 17 is amended to specifically recite that the biotinylated receptor protein is immobilized to a sensor site of a surface plasmon resonance device, a quartz-crystal microbalance, or a mass spectrophotometer, as suggested by the Examiner. New claims 44 and 45 are added to recite additional structural features associated with receptor chips adapted for detection using a surface plasmon resonance device or a quartz oscillator, respectively. Support for these amendments is provided, *e.g.*, at page 55, line 25, to page 56, line 19.

Applicants submit that claim 17, and new claims 44 and 45 dependent therefrom, satisfy the second paragraph requirements of §112 and request that this basis of rejection be reconsidered and withdrawn in light of the above amendment.

Rejection Under 35 U.S.C. § 102

Pending claims 1 and 15 stand rejected under 35 U.S.C. § 102(b) as anticipated by Holtzman *et al.* Specifically, the Examiner alleges that Holtzman *et al.* teaches a receptor chip comprising a recombinantly expressed receptor protein, TANGO 402, which is immobilized via a factor capable of specifically binding to biotin. The Examiner further asserts that while

Holtzman *et al.* does not teach the biotinylation of the receptor protein being carried out in a bacterial host, this is not given patentable weight, since it is drawn to a product-by-process.

Applicants respectfully traverse this basis of rejection and submit that the claimed receptor chip is distinct from that described by Holtzman *et al.*, since the claimed chip comprises proteins that are biotinylated *in vivo*, while those described in Holtzman *et al.* were biotinylated *in vitro*. As described in the previous Amendment submitted March 27, 2006, it is well known in the art that *in vivo* and *in vitro* biotinylation methods result in structurally distinct biotinylated proteins. Furthermore, Applicants submit that defining a product by the process of manufacturing the product is entirely acceptable, and that the patentability of the claimed product is determined in light of the structural characteristics of the product resulting from the recited process. See, *e.g.*, MPEP 8th ed. § 2113.

However, in order to expedite prosecution of the instant application, and in light of the telephone conference with the Examiner, claim 1 is amended to recite the feature that the receptor protein comprises a biotinylation sequence motif. Support for this amendment is provided, *e.g.*, at page 51, lines 12-16 and page 23, line 22 to page 24, line 3. Applicants submit that Holtzman *et al.* clearly fails to teach a receptor chip comprising a receptor protein containing a biotinylation sequence motif. Accordingly, Holtzman *et al.* cannot anticipate the presently claimed receptor chip, since it does not teach each element of the chip. In light of this amendment, Applicants respectfully request that the Examiner reconsider and withdraw this basis of rejection.

Rejections Under 35 U.S.C. § 103

Claim 16 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Holtzman *et al.* as applied to claim 1, in view of Moriwaki *et al.* More specifically, the Examiner alleges that Holtzman *et al.* teaches a receptor chip comprising an immobilized receptor protein of the LDL receptor related protein family, but concedes that Holtzman *et al.* does not teach the receptor protein being LOX-1. The Examiner asserts that Moriwaki *et al.* remedies this deficiency by teaching that the receptor protein of LOX-1 binds to a protein moiety of Ox-LDL and may be used to define ligand specificities of LOX-1. The Examiner concludes that it would have been obvious to immobilize LOX-1 on the receptor chip of Holtzman *et al.*, in

order to provide a more efficient testing surface for performing automated binding assays and facilitating the separation of complexed and uncomplexed forms of LOX-1.

In addition, claim 17 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Holtzman *et al.*, as applied to claim 1, in view of Duffy *et al.* The Examiner alleges that Holtzman *et al.* teaches a receptor chip comprising an immobilized receptor protein adapted for ELISA detection, but concedes that Holtzman *et al.* does not teach a receptor chip adapted for detection by mass spectrometry. The Examiner asserts that Duffy *et al.* teaches adapting a surface for use with ELISA or SPR. The Examiner asserts that it is well known in the art that ELISA detection is functionally equivalent to SPR detection, so it would have been obvious to substitute SPR detection, as taught by Duffy *et al.* for ELISA detection, as taught by Holtzman *et al.* In addition, the Examiner contends that such a substitution would be motivated based upon economics and availability of detection equipment.

Applicants traverse these bases of rejection and submit that neither combination of references renders obvious the claimed receptor chips, since neither of the cited combinations of references teaches or suggests each element of the claimed invention. Specifically, as described above, Holtzman *et al.* fails to teach a receptor chip comprising a receptor protein containing a biotinylation sequence motif, as recited in claim 1 and, thus, claims 16 and 17 that depend therefrom. Neither Moriwaki *et al.* nor Duffy *et al.* remedy this deficiency, since neither of these references describes a receptor protein containing a biotinylation sequence motif. Accordingly, these combinations of references clearly fail to render the claimed receptor chips obvious.

In addition, even assuming *arguendo* that one of the cited references taught advantages associated with *in vivo* biotinylation, a person having ordinary skill in the art would have no reasonable expectation of achieving the presently claimed invention with any reasonable expectation of success. As detailed in the previous Amendment submitted March 27, 2006, absent the present application, a person having ordinary skill in the art would not reasonably have expected to recombinantly produce a biotinylated receptor protein that is capable of binding a ligand of the receptor protein, as presently claimed, particularly in quantities sufficient to prepare a receptor chip. As described in the instant application and understood in the art, receptor proteins are membrane proteins and, therefore, do not lend themselves to recombinant

production in a soluble form capable of binding to a ligand. Rather, the hydrophilic properties of receptor proteins cause them to accumulate as inactive aggregates, *i.e.*, inclusion bodies, during recombinant production (*see*, page 3, lines 8-26). It is the present invention that provides methods of recombinantly expressing a biotinylated receptor protein comprising a biotinylation motif, which is capable of binding to a ligand when immobilized on a receptor chip. Accordingly, the skilled artisan would have no reasonable expectation of successfully producing the presently claimed receptor chip comprising a receptor protein that was biotinylated *in vivo* and is capable of binding a ligand of the receptor protein, absent the teachings of the instant application.

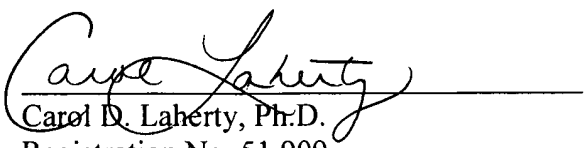
Applicants respectfully request that the Examiner reconsider and withdraw these bases of rejection in light of the above amendments and remarks.

Conclusion

In view of the above amendments and remarks, allowance of claims 1, 15-17, 54, and 55 is respectfully requested. A good faith effort has been made to place this application in condition for allowance, in light of the telephone interview conducted with the Examiner. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the same.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



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